A RETROSPECTIVE COHORT STUDY:

THE DIRECTLY OBSERVED TREATMENT SHORT-COURSE STRATEGY (DOTS) AND TUBERCULOSIS TREATMENT OUTCOMES AT VRYHEID DURING 2007: FACILTY VERSUS COMMUNITY BASED DOTS

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DECLARATION

I, the undersigned, hereby declare that the work contained in this thesis is my own, original work and that I have not previously submitted it – entirely or in part- to any university for a degree

Signature……. **Date: 24August 2009**

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ABSTRACT

1. BACKGROUND AND SETTING

The study was conducted at Vryheid in the Kwazulu-Natal province. The increasing number of TB patients at Vryheid hospital's OPD and wards has prompted me to assess the effectiveness of TB treatment by comparing the treatment outcomes between community-based DOTS (COMDOTS) and facility-based DOTS (FACDOTS). 2 main primary health care clinics were selected for the research (Bhekuzulu and Mason clinics).

2. AIM

This thesis evaluated the effectiveness and efficacy of DOTS strategy by comparing the outcomes of tuberculosis treatment of patients under DOTS at VRYHEID during 2007: facility based versus community based DOTS.

3. METHODS

The research question of the study was "Does community-based DOTS offer better TB treatment outcomes than the facility-based group?
This is a retrospective cohort study with a total sample size of 809 patients; retrieved from the records of 2 major clinics at Vryheid (TB registers) during 2007. A sample of 396 patients was required in each group to determine a difference of 10 % (with a power of 90%) between the two groups of the study: community-based versus facility-based. Mason clinic has mostly patients on facility-based DOTS whereas the patients involved in community-based approach were found at Bhekuzulu clinic.

4. RESULTS

The 2 groups of the study (COMDOTS and FACDOTS) were comparable in terms of age and gender composition.
52% of patients in the community-based group completed their TB treatment and only 37.7% in the facility-based group.
14% of patients died in the community-based DOTS group versus 6.1% in the facility-based group.

4.5% of community-based group defaulted medications, as compared to 1.7% in the facility-based group.

34.8% of facility-based DOTS interrupted treatment whereas the percentage is lower in the community-based group (1%).

The community-based group had a failure rate of 6% versus 3.7% in the facility-based.

The majority of patients in both groups were diagnosed on the basis of X-rays (82% in the community- and 57.1% in the facility-based group).

Patients for whom an HIV test result was available were extremely likely to be HIV positive in both groups (80% in the facility-based and 84.6% in the community-based group), however the number of available test results was low.

Amongst the sputum-positive patients, the community-based group was shown to have a cure rate of 95 percent (versus 37.1% in the facility-based group).

Patients in the community-based group remained longer on TB treatment than the ones in the facility-based group (5.7 vs 5.0 months). However, the community-based group had a higher percentage of retreatment cases (22.4% versus only 12.7% in the facility-based group).

5. CONCLUSION:

This study suggests that community-based DOTS offers a better cure rate (95%) and completion of therapy (52%). The longer duration of treatment observed in the community-based group could be partly due to its relatively higher number of retreatment cases as compared to facility-based group.

An extremely high HIV rate (> 80%) has also been found in the TB-patient population in both groups.

Community-based DOTS offers an alternative way for patients who do not have easy access to the clinics, provided the government strengthens the system and takes over recruitment as well as monitoring and motivation (incentives) of community-health workers.

There is also a growing concern with the relatively high number of patients defaulting or failing treatment in this group and further studies are needed particularly .retrospective to explore the matter.

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1. INTRODUCTION, BACKGROUND AND MOTIVATION

The KWAZULU NATAL (KZN) Province is the epicentre of South Africa's HIV/AIDS epidemic as well as of a severe form of tuberculosis (TB). The tuberculosis prevalence in the province is now beyond epidemic proportions.

In 2006, a study conducted at Tugella ferry (a rural small town in KZN) provided the following results: TB Sputum cultures were performed on 1,539 patients with 542 (35%) positive and 995 (65%) negative cultures. 221 (40%) patients were diagnosed with multi-drug resistant (MDR-TB) and 53 patients (24%) among MDR-TB were extensively drug-resistant tuberculosis (XDR-TB) [1].

Up to the year 2007, more than 1,000 TB cases per 100,000 people have been recorded in the province. "Any ratio of more than 200 cases per 100,000 people is regarded as an epidemic".[2]

KZN is facing an epidemic of complicated tuberculosis never seen in South Africa.

This alarming and explosive situation emphasizes the need for a comprehensive plan to successfully tackle and halt this epidemic. The increasing number of tuberculosis cases seen at Vryheid hospital's OPD and Medical wards (50 or more cases every month: new, defaulters and complicated Tuberculosis) has prompted me to indirectly assess the effectiveness of community-based directly observed treatment short - course strategy (DOTS) by comparing the outcomes of the 2 types of DOTS: community- versus facility-based DOTS. Some authors consider community-based DOTS to be a better approach for complicated tuberculosis.

1.1. DEMOGRAPHY

The study was conducted at 2 major primary health care clinics: BHEKHUZULU and MASON Clinics situated at VRYHEID. VRYHEID is a small town in the ABAQULUSI municipality in the ZULULAND district. It lies southward along the R33 in the valley at the foot of the Zungwini Mountain. It is the centre of coal mining and cattle farming in the district. Vryheid has an urban population of 24,670 and is Zululand's main commercial, industrial and business centre, with a reasonably well-developed physical, social and institutional infrastructure. It is well located at the intersection of

the major transport routes, which traverse the region. The population of Vryheid has a gender profile of 52.35 % male and 47.65 % female, with a poverty level of 32.8 %. It has an unemployment rate of 59.4%, with only 15.59 % working class.

1.2. DOTS

The directly observed therapy strategy is defined as a strategy to ensure patient compliance where a health worker or the designated person (community health worker) watches the patient swallow each dose of prescribed drugs.
In 1980, Karel Styblo developed the essential components of DOTS [6]

The 5 components of the WHO'S DOTS strategy are

1. Political and administrative commitment.
2. Case detection, primarily by microscopic examination of sputum of patients presenting to health facilities. Access to quality- assured TB sputum microscopy for case detection among persons presenting with constitutional symptoms of TB. Special attention should be paid to case detection (TB) amongst HIV infected patients and other high risk groups such as household contacts of infectious patients and people in institutions.
3. Standardized short-course chemotherapy to all cases of TB, given under direct supervision and patient support (DOT). It is called "proper case management". The SA Tuberculosis Control Programme recommends 6 months therapy for newly diagnosed TB patients. The duration of 8 months is the standard for TB retreatment or treatment failure, daily streptomycin injections are added for the initial 2 months of treatment. TB drugs are taken 5 days per week.[26]
4. Adequate supply of good quality drugs: uninterrupted supply of quality-assured drugs with reliable drug procurement and distributions systems
5. Systemic monitoring and accountability for every patient diagnosed; recording and reporting systems are crucial for the evaluation of the outcomes of every TB patient, and for the assessment of the overall programme performance. It forms the backbone of a systematic programme monitoring and resolution of identified problems.

The aims of DOTS are summarized as follows:

- Cure rates of up to 95%
- Prevention of MDR/XDR TB emergences.
- Improvement of quality of life and longevity of AIDS patients by TB control.

South Africa (SA) has started the implementation of its DOTS program in 2001.
MDR/XDR TB constitutes a growing threat to the global control of tuberculosis and impacts negatively on health workers as well as families and communities at large. Treating MDR/XDR tuberculosis is costly in terms of hospital stay and medications. In February 2008, the World Health Organization released its fourth global report on anti-TB drug resistance, which indicated that the number of MDR TB cases worldwide was increasing and the highest ever reported (489,139 cases in 2006) and that XDR TB had been reported in 45 countries. A critical need exists for new drugs and new drug regimens to address this growing challenge with emphasis on a comprehensive and integrated approach. The Global Alliance for TB Drug Development, of which CDC is a member, continued to make progress in this area in 2007, with new candidate drugs moving forward in clinical trials. The WHO has recommended the application of the DOTS strategy for prevention of complicated tuberculosis in developing countries.

2. AIMS AND OBJECTIVES

2.1. AIM

To evaluate the effectiveness of DOTS strategy by comparing the outcomes of tuberculosis treatment of patients under DOTS at VRYHEID during 2007: facility-based versus community-based DOTS.

2.2. OBJECTIVES

1. To determine the cure rate of patients under DOTS at Vryheid during 2007.
2. To evaluate and compare the treatment outcomes between community-based and facility-based DOTS at Vryheid.

3. OVERVIEW OF THE LITERATURE REVIEW

Tuberculosis is an important cause of death in the world. One of the major reasons for failure of tuberculosis treatment in African nations has been poor compliance with therapy, with resulting low treatment completion and cure rates. It is the leading killer of HIV-infected Africans. Tuberculosis can be controlled by applying the WHO's directly observed therapy, short-course (DOTS) strategy. This strategy is aiming at detecting at least 70% of new smear positive tuberculosis cases and curing at least 85% of these. DOTS strategy was described by WHO at its introduction as the most important public health breakthrough of the decade in terms of lives saved. It is also one of the most" cost-effective of all health interventions" according to World Bank. Application of the WHO DOTS strategy can prevent drug-resistance [3;]

Two types of DOTS have been described: the facility-based DOTS (FACDOTS) and the community-based DOTS (COMDOTS)

The FACDOTS is defined as the observation of the intake of tuberculosis drugs at the health facility by a health worker. It is referred to as the conventional method. In contrast, community-based DOTS (COMDOTS) is the administration of TB drugs by a trained member of the community. The latter approach was introduced to overcome some of the adherence barriers such as accessibility and as an attempt to improve the cure rates of tuberculosis treatment. Limited studies conducted in South Africa and Tanzania did not show much difference between these types in terms of treatment outcomes and cure rates, calling for further studies.[4; 5]

3.1. TB and HIV

HIV-infected individuals are at least 30-fold more likely to develop reactivation tuberculosis as HIV progresses .They are also more susceptible to exogenous infection in populations with a high prevalence of tuberculosis. Active tuberculosis accelerates the natural dynamics of tuberculosis epidemics. The risk of developing tuberculosis in HIV infected adults is 3 to 8% annually, giving a cumulative lifetime risk of 80% or more. In sub-Saharan Africa, 20 to 70% of all new adult cases and 10

to 40% of children with TB are HIV infected. The interaction of tuberculosis and HIV-infected individuals is associated with increased HIV replication, possibly mediated by enhanced expression of pro-inflammatory cytokines such as tumour necrosis factor- alpha. Reactivation of latent tuberculosis is believed to be the major mechanism leading to tuberculosis in HIV-infected persons. HIV is the most important known risk factor for progression from latent TB infection (LTBI) to TB disease. The Centers for Disease Control and Prevention (CDC - a United States federal agency under the Department of Health and Human Services based in Atlanta) recommend routine screening for HIV for all persons with TB or LTBI at the initiation of TB or LTBI treatment[11]. The CDC continues to work with domestic and international partners to increase awareness of TB/HIV co-infection and improve the integration of TB/HIV health-care services. In many African countries, half or more of tuberculosis patients are now infected and it is important to note that persons with HIV infections are at increased risk of rapid progression following primary infection or re-infection, and also from reactivation of latent infection with Mycobacterium tuberculosis. More strategies are needed to curb the HIV transmission (active and passive case detection; prevention of nosocomial transmission) and reactivation (preventive therapy). The high burden of other HIV related disease in patients with tuberculosis, such as other bacterial infections, toxoplasmosis and other manifestations of AIDS, requires a well integrated TB-HIV/AIDS program including the provision of HIV/AIDS care. HIV/AIDS in Africa poses severe challenges of purpose and identity to tuberculosis control programmes, which have not adapted to the altered realities of the HIV/AIDS era.

HIV infection could rapidly become a risk factor for drug-resistant TB if HIV infected patients become co- infected with drug-resistant mycobacterium tuberculosis or if HIV infections become a risk factor for acquired resistance as the co-epidemics evolve. Therefore efforts to prevent active TB in the large population of persons infected by TB and HIV co-epidemics through the use of preventive should be pursued. Policy makers in low income countries with TB and HIV co-epidemics should maintain investment in DOTS implementation but should also realise that TB case fatality rates will continue to rise and that program performance may be better judged using rates of drug resistant TB[6].

A well implemented DOT strategy amidst rapidly increasing prevalence of HIV in sub Saharan Africa may succeed in controlling drug resistant TB but may fail to control the TB case rate. The apparent ineffectiveness of the current DOTS strategy in lowering TB rates in the population is likely due to the fact that most of the TB cases now result from endogenous reactivation of latent tuberculosis in HIV infected persons. The role of DOTS in controlling the TB case rate in the era of HIV is to convert TB cases to a non-infectious state as soon as possible in order to reduce transmission especially to HIV infected. DOTS, however, cannot prevent development of active TB in persons who were infected with Mycobacterium Tuberculosis many years earlier[6].

3.2. DOTS AND DRUG-RESISTANT TUBERCULOSIS

Multi-drug resistant tuberculosis (MDR-TB) is a growing hazard to human health world wide and threatens the control of tuberculosis. It is a man-made problem and its emergence can be prevented by prompt diagnosis and effective treatment of all TB cases. Adoption of directly-observed therapy short course (DOTS) to prevent the resistant/ multi-drug resistant strains and careful introduction of second line drugs to treat patients with MDR-TB are the top priorities[5]. Standard short course chemotherapy, based on first line drugs, is inadequate for some patients with drug-resistant tuberculosis TB. Therefore it should be modified in some settings to identify drug-resistant case sooner and to make use of second-line drugs in appropriate treatment regimens. The emergence of MDR is also a symptom of ineffective tuberculosis control. Moreover, the treatment of MDR-TB is difficult, expensive and requires prolonged therapy with more toxic second-line drugs which are not available at most tuberculosis control programs in developing countries [7; 8].

The development of the DOTS strategy is a milestone in tuberculosis (TB) control at the global and national levels but it is challenged by the following weaknesses which need to be overcome: built on case management, sustaining commitment, competing priorities, the threat of HIV, maintaining high quality of care and preventing drug resistance, building human resource capacity, improving diagnosis and fostering operations research. The ability to address these challenges will determine the success or failure of the Global Plan to Stop TB 2006 - 2015 [8; 9; 10].

The treatment success with WHO DOTS strategy was 83 % of the world's population living in countries or part of countries covered by this strategy by the end of 2004 but could not reach the target of 85 %. In the 2003 DOTS cohort study, treatment success was below average in the African Region (72%), which can be partly attributed to occurrence of HIV co-infection, and in the European Region (75%), partly due to drug resistance. Drug resistance, specifically multidrug resistance and extensive drug resistance, is a serious threat to public health in all countries, especially where the highest rates of multidrug resistance are presently accompanied by a rapid increase in HIV infection. Based on the experience of the first projects approved by the Green Light Committee, the treatment success of patients with multidrug-resistant tuberculosis (MDR-TB) is lower than that of drug-susceptible cases, but nevertheless reaches 70%. The collaborative effort of different organizations, professionals and communities is needed to address the development and spread of multidrug resistance and extensive drug resistance, which combined with the epidemic of HIV infection is one of the barriers to dealing effectively with TB. This effort should be directed towards facilitating the diagnosis and treatment of TB patients, in particular by improving access to drug susceptibility testing and strengthening treatment delivery by rigorous adherence to DOTS as outlined by the Stop TB Partnership [9, 10]. DOTS constraints include: problems with health facilities, patients, drugs and the disease itself. The effective involvement of private healthcare providers is imperative to achieve better geographical and patient coverage for the implementation of DOTS.[10]

The strong association between HIV and TB in sub-Saharan Africa is responsible for the massive increase in the incidence of TB observed in this region in the last 20 years. Diagnosis of TB in resource-poor countries is largely based on sputum-smear microscopy and chest radiography, although these methods lack sensitivity or specificity, especially when used on HIV-infected patients. Unfortunately, countries in sub-Saharan Africa are falling short of the World Health Organization's targets for case detection and treatment. This failure is, in turn, making the achievement of the Millennium Development Goals for TB--to ensure that the incidence of TB is falling by 2015 and to halve the prevalence of TB and the annual number of TB-attributable deaths between 1990 and 2015-less likely. To improve the performance and impact of TB-control programs, in the face of HIV co-infection and other constraints on

DOTS, the World Health Organization has launched " *the revised Stop TB Strategy*". The new strategy, to be implemented via the Global Plan to Stop TB (2006-2015), includes intensified TB-case finding, treatment of latent TB infection with Isoniazid, prevention of HIV infection, cotrimoxazole preventive therapy, and antiretroviral therapy[10; 11; 12; 13].

The DOTS- Plus strategy for the management of Multi-drug resistant (MDR)-TB and the establishment of The Green Light Committee to review project applications in this area are also initiatives taken to curb the problem of drug-resistance. Treatment of MDR-TB is difficult, complicated, expensive, challenging and needs skills and experience. All measures should be taken to persuade and encourage patients not to stop treatment despite its discomforts to prevent morbidity, mortality and transmission of MDR-TB. The current proposal of the WHO DOTS plus highlights the need for a comprehensive management strategy to control MDR-TB. The adoption of DOTS to prevent the resistant/ multi-drug resistant strains and careful introduction of second line drugs to treat patients with MDR-TB are the top priorities for the proper control of MDR-TB. A DOTS alone is unlikely to control tuberculosis in sub-Saharan Africa; however one major achievement of the implementation of DOTS is to limit the development and spread of drug-resistance.

It is also important to note that women are at increased risk of progression to disease during their reproductive years. The fear and stigma associated with tuberculosis have a greater impact on women; often leaving them in a more precarious social and economic position[25]. Tuberculosis in women creates orphans, impoverished families and reduces the economic development of society. Gender differentials exist in reporting and diagnosing TB and passive case finding likely leads to failure to diagnose TB in women. Therefore, Tuberculosis Control programs should be sensitive in the constraints faced by women in accessing health care, in order to empower women to commence and complete treatment[25].

4. STUDY DESIGN AND METHODOLOGY

4.1. RESEARCH QUESTION

Does Community-based DOTS strategy offer better tuberculosis treatment outcomes than the facility- based DOTS program?

4.2. STUDY DESIGN

It is a retrospective (non concurrent or data base) COHORT study.

The research was conducted at (data were retrieved from the TB registers at) BHEKUZULU and MASON Clinics, in VRYHEID at ABAQULUSI municipality. The study looked at the cure rate and outcomes of tuberculosis treatment of patients under DOTS strategy at VRYHEID: facility- versus community based-DOTS.

It is an observational assignment study as patients were already allocated to community- and facility-based DOTS at the time of extraction of data.

The following main outcomes were assessed: cured, completed, defaulted, relapsed, failed, and died.

5. SAMPLING, DATA COLLECTION AND ETHICAL CONSIDERATIONS

5.1. SAMPLING

The study was conducted at VRYHEID, in the Kwazulu-Natal province and data were collected from TB registers of 2 primary health care facilities (Mason and Bhekuzulu clinics) from January to December 2007.

The diagnosis is usually made at the clinics or at Vryheid hospital and patients were thereafter assigned to one of the 2 groups of the study, based on their location or access to the health facility (near to or far from the clinic) and the preference of the patients. In both, facility- and community-based groups, patients collected their medications at their assigned clinic on a monthly basis. However, in the community-based group, patients are visited by the community health workers on a weekly basis to count the pills, double check the ticking process, discuss patient's problems and report back to the mother clinics. Daily supervision of TB drug-taking (5 days per week) and ticking of the green TB card is done by family members or by the patients themselves.

The severe shortage of community health workers versus vastness of areas to cover has made the coverage of all catchment areas by community health workers difficult. Therefore there are some patients who opted for community-based DOTS and who are visited by mobile clinics monthly.

It is sad to note that community health workers were recruited and paid by non-governmental organizations and attached to the clinics. Clinics operational managers were adamant to the fact that not only they did not have control on community health workers activities but also that some of the community health workers did not do their jobs properly (e.g. regular visits to patients) because other commitments such as attending to their own lucrative jobs. Serving 2 masters resulted in poor supervision of patients. It is also important to mention that community health workers were not regularly up-skilled.

Patients on retreatment (after cure, relapse or failure) regimen received their daily injection of streptomycin (5 days per week) at the clinics for the first 2 months of the treatment and may thereafter continue either in a facility- or a community-based group.

Following criteria were used in sampling patients for the research:

Inclusion criteria:

- Age : children and adults

- Sex: Female or male
- Newly diagnosed, relapse, treatment failure or defaulting
- Pulmonary or extra-pulmonary tuberculosis

Exclusion criteria:

- Confirmed MDR/XDR patients on therapy, because these patients are admitted and treated in specialized centers where strict facility-based DOTS are applied.

A sample size of 392 (N=392) patients for each group was estimated to be needed to determine a difference of 10 % (with a power of 90%) between the two groups of the study: community-based versus facility-based DOTS.

5.2. DATA COLLECTION

The data for the study were extracted from the two clinics' TB registers by clerks. The clerks did not receive any specific training for this study, but worked hand in hand with the TB coordinator nurse and were bound to confidentiality.

The data collection sheet included the following information:

- Code
- Age
- Gender: female or male
- Duration of treatment
- HIV status (if available)
- TB Status: newly diagnosed, retreatment after cure, default, failure and other types
- Treatment outcomes: completed, cured, failure, default, lost to follow-up, died, transferred, moved out, interrupted
- Diagnosis mode: Sputum AFB , CXR results, biopsy
- Sputum microscopy, culture and sensitivity results.

The study included 809 patients, with 401 patients retrieved from Mason and 408 from Bhekuzulu clinic.

The South African National Tuberculosis Control Programme provides the following definitions of concepts used in TB treatment outcomes:

- Cured (C): defined as patient who initially was smear positive, converted to a smear negative at or 1 month prior to completion of treatment and on at least on one previous occasion.

- Treatment Completed (TC): patient who has completed treatment but does not have bacteriologic proof of cure.

- Treatment Defaulted (TD): a patient whose treatment is interrupted for 2 consecutive months or more.

- Treatment Failure (TF): patient who remains smear-positive at 5 months or later during treatment.

- Died (D): patient who dies for any reason during TB treatment.

- Treatment interrupted: when TB treatment has been interrupted for less than 4 weeks.

- Transfer out: when a TB patient has been transferred to another sub-district health district, province or country and for whom treatment outcome is not final.

- Moved: when a TB patient has moved from one health facility to another within the same sub- district. This outcome is not counted as final.

5.3. DATA ANALYSIS

The CHI-SQUARE, MANN-WHITNEY and ANOVA tests were used and assisted in comparing the 2 modes of DOTS, focusing specifically on the cure rate and the outcomes of TB treatment.

5.4. ETHICAL CONSIDERATIONS

Confidentiality and privacy of patients were observed by using a coding system. Only the TB clerks at the site of collection of data had access to these records

A waiver for informed consent was obtained from the ethics committee of Stellenbosch University as well as approval from the KZN health authorities.

6. RESULTS

The study was conducted at Bhekuzulu and Mason clinics. Vryheid TB clinic was not part of the study, as its 2007 TB-register was missing at the time of collection of data.

A sample of 392 patients in each group was aimed for.

Altogether 809 cases were included in the research, with 401 at Bhekuzulu clinic and 408 at Mason clinic.

6.1. DEMOGRAPHIC CHARACTERISTICS

The following demographic parameters were considered in the study:

- Age
- Gender
- HIV status
- Mode of Diagnosis
- TB status or category

N.B. The residuals (observations minus the DOT group mean) in the analysis of age and duration of treatment are not normally distributed. Therefore the results from non-parametric tests (i.e. the Mann-Whitney tests) will be used to analyze the 2 variables

Table 1. AGE DISTRIBUTION

	All patients Mean(CI 95%)	Facility based Mean (CI 95%)	Community based Mean (CI 95%)	P value
Age (years)	30.6 (29.5-31,7)	31.2 (29.7-32.6)	30.1 (28.5 – 31.6)	0.30

The comparison of age between the 2 groups of the study has shown no significant difference (p value = 0.30).

Table 2. MANN-WHITNEY TEST FOR AGE

Variable	Mann-Whitney U test :by variable DOTS type Marked tests are significant p <0.05						
	Rank Sum community	Rank Sum facility	U	Z adjusted	p- level	Valid N Community	Valid N Facility
Age	161584.5	166060.5	80983.50	-0.246833	0.865037	401	408

In addition to the chi-square test, the Mann-Whitney test was used as there was no homogenous distribution of age. The Mann-White test has also confirmed the lack of difference between the 2 groups.

Table 3. GENDER DISTRIBUTION

		All patients		Facility based DOTS		Community based DOTS		P value
		N	%	N	%	N	%	
GENDER	Female	400	49.4	191	46.8	209	52.1	0.13
	Male	409	50.6	217	53.2	192	47.9	

The community-based DOTS had 52.1 percent of male patients and 47.9 of female involved in the study, whereas 46.8 percent were male patients and 53.2 percent female in the facility-based DOTS.

The study did not show any major difference between the 2 groups that could affect the results (p value= 0.13)

Table 4. HIV STATUS AND MODE OF DIAGNOSIS

		All patients N= 809		Facility Based N= 408		Community based N= 401		P value
		N	%	N	%	N	%	
HIV status	Known	148	18.3	5	1.2	143	35.7	< 0.01
	Unknown	661	81.7	403	98.8	258	64.3	
HIV rate (of those tested)	Positive	125	84.5	4	80	121	84.6	
	Negative	23	15.5	1	20	22	15.4	
DIAGNOSTIC MODE	CHEST X-RAYS	564		233	57.1	331	82.5	
	SPUTUM	244		175	42.9	69	17.2	0.0000

- 35.7% of patients involved in community-based DOTS had their HIV tests done but the testing rate in facility is only 1.2%. It is also important to note that both groups had a high rate of unknown results (98.8% in facility- and 64.3% for community-based). The difference in the testing rate between the 2 groups is statistically significant (p= < 0.01)

- In the community-based treatment group, a significantly smaller percentage of patients had been diagnosed with positive sputum (17.2% versus 43% in the facility-based treatment group). The majority of cases in both groups was diagnosed on grounds of chest x-rays (82.5% in the community group, 57.1% in the facility-based group)

Table 5. TB STATUS (CATEGORY)

	Community- based group	Facility- based group	Total
	N (%) 401	N (%) 409	809
New cases	311 (77.6%)	356 (87 %)	667 (82.4)
Retreatment cases	90 (22.4%)	52 (13%)	142 (17.6)

The community-based group had 77.6% new cases and 22.4% of retreatment but the number of retreatment is smaller in facility-based (87% new cases and 13% retreatment cases).

6.2. OUTCOMES OF TUBERCULOSIS TREATMENT

In this section 3 categories of results will be presented:

- Outcomes of TB treatment
- Tuberculosis cure rate
- Duration of TB treatment

Table 6. TB TREATMENT OUTCOMES

	Community based group	Facility based group	All patients	P value
	N= 401 N (%)	N= 408 N (%)	N= 809 N (%)	significant if < 0.05 (*)
Cured	66 (16.5)	65 (16.2)	131 (16.2)	0.93038
Completed	209 (52.1)	154 (37.7)	363 (45)	0.00389*
Defaulted	18 (4.5)	7 (1.7)	25 (3.1)	0.02781*
Died	57 (14.2)	25 (6.1)	82 (10.1)	0.00041*
Failed	24 (6)	15 (3.7)	39(5)	0.14954
Retreatment after cure	3 (0.7)	0	3 (0.4)	
Lost- to follow-up	7 (1.7)	0	7 (1)	
Moved	11 (2.7)	0	11 (0.1)	0.00091*
Transferred	2 (0.5)	0	2 (0.2)	
Interrupted	4 (1)	142 (34.8)	146 (18)	0.00000*

Table 5 compares the outcomes of TB treatment within the group and between the 2 groups.

- 52% of patients in community-based completed their TB treatment and only 37.7% in facility group.
- 14% of patients died in community-based DOTS versus 6.1% in facility-based group
- 4.5% of community-based group defaulted medications as compared to 1.7% in facility group.
- 34.8% of facility-based DOTS interrupted treatment whereas the percentage is lower in community-based (1%)
- Community –based group had a failure rate of 6% versus 3.7% in facility.

Table 7. TUBERCULOSIS CURE RATE

	Community based	Facility based	Total
Cured (i.e. sputum negative at 5 or 6 months of therapy)	N= 66	N= 65	131
Total sputum positive at the beginning	69	175	244
Cure rate	95.65 %	37.14%.	

The cure rate (in percentage) is calculated as follows:

Cure rate (%) = Total number of sputum negative at 5-6 months of TB treatment

Total number of sputum positive at onset of TB therapy.

Community-based treatment group has shown to have a higher cure rate (95.65%) as compared to facility-based DOTS (37.14%).

Table 8. DURATION OF TREATMENT

	All patients Mean (CI 95 %)	In Facility Mean (CI 95%)	In Community Mean (CI 95%)	P value
Duration of treatment (months)	5.35 (5.2- 5.5)	5.01 (4.8- 5.2)	5.7 (5.5- 5.9)	0.00003

It is important to note that duration of treatment means the effective duration of treatment including drop-outs by deaths or loss-to-follow-up.

The table above shows that patients in the community-based group on average remained significantly longer on treatment than those in the facility-based.

Table 9. MANN-WHITNEY TEST FOR DURATION OF TREATMENT

Variable	Mann-Whitney U test :by DOTS type Marked tests are significant p <0.05						
	Rank Sum community	Rank Sum facility	U	Z adjusted	p- level	Valid N Community	Valid N Facility
Duration	179908	147737.	64301.00	5.454186	0.0000	401	408

This test addresses the lack of a normal distribution in the duration of treatment as demonstrated by other tests.

P value is 0.0000 for duration of treatment; meaning that there is a significant difference between the 2 groups.

7. DISCUSSION

7.1. MAIN FINDINGS

7.1.1. Duration and outcomes of TB treatment

Community-based DOTS has shown to have a higher cure rate (96.5%), a higher number of patients who have completed TB therapy (n= 209) and a higher mean duration for treatment (5.7 months).

Achieving a cure rate up to 95 percent is one of the aims of the DOTS strategy as outlined by the WHO at its introduction. COMDOTS with its 96.5% has performed beyond the expectation.

There are, however, some confounding factors concerning the duration of treatment. The community-based group in the study was shown to have 22.4% of retreatment cases versus only 13.6% in the facility-based group. Since the retreatment-cases are supposed to receive a longer treatment according to the national protocol (8 versus 6 months), this might affect the resulting average treatment duration.

In both groups medications (TB-drugs) are dispensed on a monthly basis, but patients take their drug 5 days per week, supervised mostly by family members or themselves who ticked on the green card. It is important to note that in the community- based group patients are visited by community health workers on a weekly basis to discuss their concerns, and a feedback report is given to the mother clinic every week. Patients who were assigned to the community-based group and who live in an area hard to reach benefit from a monthly mobile clinic visit to address their concerns (such as side effects, counting of pills, ticking of cards, change of regimen and referral). Investigations are done at the end of the intensive and of the continuation phase or at any other time the need arises.

The weekly visit to patients, for support, motivation and discussion of their concerns by community health workers in the community-based group may play a vital role in the achievements noticed in this group. However, it is important to note that community health workers who have other lucrative jobs and may not have time to visit patients regularly could either underreport or exaggerate some of the figures, which will distort the true impact of community-based DOTS.

It is important to note that in either group, patients who were diagnosed with treatment failure, relapse or who previously had defaulted treatments were initiated on the 2nd-line regimen according to the South African national tuberculosis programme guidelines, while sputa specimens were collected and sent to the laboratory for further analysis (microscopy, culture and sensitivity). Ambulatory patients received injections of streptomycin at the clinic for the initial 2 months, whereas very sick and non-adherent patients were admitted to Vryheid district hospital for a short stay while transfer arrangements to nearby hospitals with TB ward facility (MOUNTAIN VIEW and SILOE hospitals) were made.

Confirmed MDR patients and suspected XDR patients were admitted at THULASIZWE hospital (specialized TB hospital), where they received supervised (health workers) and specialized TB treatments. Confirmed XDR patients were directly sent to the special TB unit of King George Hospital in Durban.

However, the study shows that community-based DOTS is also associated with a 4.5 percent rate of defaulters versus 1.7 percent in the facility-based group with treatment failure rate is a bit higher in the community-based (6%) as compared to the facility-based group (3.7%).

Lastly, the community-based group has shown a drastically lower treatment interruption rate (1%), compared to the facility-based group (34.8%).

7.1.2. Age and Gender distribution

Age and gender were fairly distributed between the 2 groups of the study and no significant difference in age and gender between community and facility- based DOTS has been shown. Patients in the community group had a mean age of 30 years versus 31 in facility.

46.8 percent of female and 53.2% of male patients were recorded in the facility-based group versus 52.1% of female and 47.9% of male patients in the community-based group.

7.1.3 Mode of diagnosis of Tuberculosis

There is a significant difference between the 2 groups of the study in relation to the mode of diagnosis. Nevertheless, it is important to note that TB patients were diagnosed (CXR, sputum or other means) at Vryheid hospital and down-referred via Vryheid Hospital's TB clinic to a primary health care clinic for commencement of treatment. The choice of clinic is based on the location and preference of the patient.

7.1.4. HIV status

The difference in the number of patients tested for HIV status between the 2 groups is due to an administrative fall-out (lack of HIV status column in the 2007 TB register).

However, the high rate of HIV (>80%) in those patients with documented HIV results is in line with the high rate of immuno-suppression that has to be expected given the above described modes of diagnoses (chest X-rays/ clinical rather than sputum).

7.2. COMPARISON WITH OTHER STUDIES

This study suggests that community-based DOTS offers better TB treatment outcomes with regard to cure rate and interruptions of treatment.

These findings do not exactly match the findings of 2 previous studies[4;5] conducted in Tanzania and South Africa which concluded that there were no differences between the 2 strategies (community- and facility-based DOTS).

However, this study confirms the one of the findings of the above mentioned studies stating that community-based DOTS may constitute an alternative way of TB treatment in rural areas when distance between the facility and the community is an issue.

7.3. STRENGTHS AND WEAKNESSES OF THE STUDY

There has so far not been any study in the KZN province that has evaluated the effectiveness and efficacy of community- versus facility-based DOTS by retrospectively looking at their treatment outcomes. Therefore this study has given

an opportunity to compare TB treatment outcomes between community- and facility-based DOTS and calls for further studies in this field.

The diagnosis of tuberculosis in this study was mainly made on X-rays grounds and not on sputum as recommended by the national and international guidelines. KZN province has the highest prevalence of HIV/AIDS in the country, making the diagnosis of tuberculosis by sputum more difficult. It is important to note that both chest x-rays and sputum investigations in HIV patients, especially in those with advanced stages, lack specificity and sensitivity.

This study was conducted at 2 main clinics in Vryheid: Mason and Bhekuzulu clinics. The diagnosis is made at the hospital and patients are down-referred to these 2 clinics. Mason clinic focuses exclusively on patients who collect their medications at the facility (once per month). Bhekuzulu clinic is located in a BHEKHUZULU township in Vryheid and deals mostly (99%) with community-based DOTS. Patients are assigned to one of these clinics, based on their choice and accessibility to the health facility (distance between the clinic and their location). This type of assignment of patients could result in selection bias.

8. CONCLUSION AND RECOMMENDATIONS

1. The COMDOTS strategy seems to offer better treatment outcomes in terms of cure rate (95%) and interruption rate than the FACDOTS approach. Although patients in the community-group appeared to remain longer on treatment, it is difficult to draw conclusion on this benefit as this group of the study had a relatively higher number of retreatment cases (that may in part explain the longer duration of treatment observed). There is a need for further studies to look at reasons behind the relatively high rate of defaulters and treatment failures seen in the COMDOTS group. Community-based DOTS can also be used as an alternative way of treating tuberculosis in areas where access to the health facilities is hampered by long distances between the community and the primary health care facilities. Continuing education of patients and the community regarding the availability and potential benefits of community-based DOTS may increase the uptake of this program for patients living far from the clinic.

2. It is vital that the government takes over completely the recruitment and allocation of community health workers. This measure will not only allow the government to establish proper governance, but also a close monitoring of daily activities of community health workers. This category of staff is crucial for the success of the national TB program and should not be left in the hands of private organisations (NGO). They should report directly to the sisters-in-charge of clinics. There is also a need for motivation of community health workers and for the provision of regular in-service training to keep up with national guidelines. Again, this calls for an active involvement of the government. The recruitment and training of a large number of community health workers by the government not only will result in daily visits to patients (not just weekly), but will also ease the burdens for patients living in areas hard to reach and may reduce the number of defaulters and treatment failures. This advocates the need for a complete shift of paradigm of visits to patients: from weekly to a daily visit in order to curb the increasing number of MDR/ XDR observed in our province.

3. The facility-based DOTS should not be abandoned and can still be used for patients who are living within the neighbourhood of the clinic and are willing to collect medications at the clinic. It should be strengthened and amended to a daily

supervised swallowing of medications at the health facility. The success of the treatment and thus better outcomes should be the responsibility of both the patient and the health care provider.

4. Sputum and chest x-ray investigations, found in my study as major modes of diagnosis of pulmonary tuberculosis, have been proven to lack specificity and sensitivity in areas with high prevalence of HIV and AIDS. Therefore it is paramount for the government of SA and its national Tuberculosis program to find alternative and reliable ways of diagnosing tuberculosis in patients infected with HIV/AIDS.

5. The results of this study will be shared with the local managers, health workers and community to highlight the benefits of adhering to treatment in terms of TB management outcomes.

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10. APPENDICES

10.1. KZN HEALTH DEPARTMENT: HEALTH RESEARCH COMMITTEE APPROVAL LETTER

HEALTH
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10 – 102 Natalia Building, 330 Langalibalele Street
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Reference: HRKM023/09
Enquiries: Mr X. Xaba
Telephone: 033-395 2805

8 May 2009

Dear Dr CN Kibamba

Subject: Approval of Research

1. The research proposal titled **"The Directly Observed Therapy Strategy (DOTS) and the Tuberculosis treatment at Vryheid during 2007: Facility based versus community based DOTS"** was reviewed by the KwaZulu-Natal Department of Health. The proposal is hereby **approved** for research to be undertaken at Vryheid Hospital, Mason Street and Bhekuzulu clinics.

2. You are requested to undertake the following:
   a. Make the necessary arrangement with identified facility before commencing with your research project.
   b. Provide an interim progress reports and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za.

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr. S.S.S. Buthelezi
Chairperson: Provincial Health Research Committee
KwaZulu-Natal Department of Health

uMnyango Wezempilo . Departement van Gesondheid

Fighting Disease, Fighting Poverty, Giving Hope

10.2. STELLENBOSCH UNIVERSITY ETHICS COMMITTEE APPROVAL DOCUMENT

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot · your knowledge partner

MAILED

28 April 2009

Dr CN Kibamba
Department of Family Medicine
Stellenbosch University
Tygerberg
7505

Dear Dr Kibamba

"The directly observed therapy strategy (DOTS) and Tuberculosis treatment outcomes at vryheid during 2007: Community versus facility-based DOTS." A retrospective cohort study

ETHICS REFERENCE NO: N09/02/072

RE : FINAL APPROVAL

At a meeting of the Health Research Ethics Committee that was held on 01 April 2009, the above project was approved on condition that further information is submitted.

This information was supplied and the project was finally approved on 28 April 2009 for a period of one year from this date. This project is therefore now registered and you can proceed with the work.

Please quote the above-mentioned project number in ALL future correspondence.

Please note that a progress report (obtainable on the website of our Division: www.sun.ac.za/rds should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly and subjected to an external audit.
Translations of the consent document in the languages applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239
The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

29 April 2009 09:12

Fakulteit Gesondheidswetenskappe · Faculty of Health Sciences

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